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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,121	11/13/2001	Kevin R. McIntosh	640100-441	5983

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,121	MCINTOSH ET AL.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71,72 and 96-117* is/are pending in the application.

4a) Of the above claim(s) *72,116 and 117* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71 and 96-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 71, 72, 96-117 are pending.

1. Applicant's election with traverse of Group II, claims 71, 96 , and 98-115 in Response to the Restriction Requirement, filed 11/24/03 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the search of Groups I-IV together would not constitute a serious search burden on the examiner .

This is not found persuasive because the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria and therefore establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions are distinct for reasons elaborated in paragraphs 4-5 of the previous Office Action and above

The requirement is still deemed proper and is therefore made FINAL.

Upon further consideration the prior art search has been extended to include claims 71 , 96, 97 99-114 of Group I.

Claims 72, 116 and 117 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 71 and 96-115 drawn to a process for treating a transplant recipient to reduce in said recipient an immune response of effector cells against a xenoantigen, comprising administering to a transplant recipient mesenchymal stem cells, wherein T cells are from the donor or from the recipient and the xenoantigen is from the recipient or from the donor, are under consideration in the instant application.

2. The specification on page 1, line 7 should be amended to reflect the status of the parent 09/427,333 and 09/267,536 applications.

3. The filing date of the instant claims is deemed to be the filing date of the instant applications, i.e. 11/13/2001 , as the parent application is drawn only to a process for treating a transplant recipient to reduce in said recipient an immune response of effector cells against an alloantigen to the effector cells, and thus does not support the claimed process for treating a transplant recipient to reduce in said recipient an immune response of effector cells against a xenoantigen to the effector cells, of the instant application. If applicants disagree, applicants should present a detailed analysis as to why the claimed subject matter has clear support in the parent application.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 99, 104, 108, 109 and 110-113 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Dependent claim 99 recite the limitation "wherein said T cells are present in a transplant ". There is insufficient antecedent basis for this limitation since base Claim 71 does not recite "transplant". Base claim 71 only recite 'transplant recipient" i.e. a patient receiving a "transplant".

B. Dependent claim 104 recite the limitation "wherein transplant is skin ". There is insufficient antecedent basis for this limitation since base Claim 71 does not recite "transplant". Base claim 71 only recites 'transplant recipient" i.e. a patient receiving a "transplant".

C. Dependent claim 108 recite the limitation "wherein transplant is solid organ ". There is insufficient antecedent basis for this limitation since base Claim 71 does not recite "transplant". Base claim 71 only recite 'transplant recipient" i.e. a patient receiving a "transplant".

D. Dependent claims 110-113 all recites the limitation "wherein said mesenchymal cell are administered prior to/concurrently with/ as part of/subsequently to transplant " accordingly . There is insufficient antecedent basis for this limitation since base Claim 71 does not recite "transplant". Base claim 71 only recite 'transplant recipient" i.e. a patient receiving a "transplant".

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 71 and 96-115 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection.**

" A process for treating a transplant recipient to reduce an immune response of effector cells against a xenoantigen to the effector cells" claimed in claim 71 represents a departure from the specification and the claims as originally filed and applicant has not pointed out where the support comes from.
The specification and the claims as originally field only support " a process for treating a transplant recipient to reduce in said recipient an immune response of effector cells against an alloantigen to the effector cells".

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 71 and 96-115 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,328960. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-22 of U.S. Patent '960 recites a process for treating a transplant recipient to reduce an immune response of the effector cells against antigen, wherein said antigen is an alloantigen, comprising administering to a transplant recipient mesenchymal stem cells in a amount effective to reduce an immune response of effector cells against said alloantigen. Claims 1-22 of U.S. Patent '960 do not recites that antigen is xenoantigen. It is noted however, that alloantigen recited in claims 1 - 22 of US '960 and xenoantigen recited in the instant claims are similar in that both antigens can induce an immune response in the transplant recipient and both differ from antigens expressed by the recipient. It is obvious that US Patent '960 and present application administer the same treatment i.e. mesenchymal stem cells to achieve the same results, i.e. to reduce an immune response in transplant recipient against antigen. Therefore it would be obvious to one of ordinary skill in the art at the time the invention was made to substitute one type of an antigen i.e. an alloantigen, to another type of antigen, i.e. xenoantigen in a process for treating a transplant recipient as recited in claims 1-22 of US Patent '960. When the prior art method is the same as a method recited in the instant claims , it can be assumed the method will obviously perform the claimed process absent a showing of unobvious property.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 71 and 96-115 are rejected under 35 U.S.C. 103(a) as being obvious over WO 01/26470 A1 in view of WO 9623058.

WO'470 teaches a method for treating a transplant recipient to reducing an immune response of the effector cells against alloantigen to the effector cells, comprising administering the suppressor cells (see entire document, Abstract , page 7 lines 10-15 and claims 1-27 in particular). WO'470 teaches that effector cells are T cells (see claim 3 in particular). WO'470 teaches that it has been discovered that mesenchymal stem cell (MSC) can induced antigen-

activated T cells to become suppressive for said antigen response and that human suppressor cells can be used in transplantation to ameliorate a response by the immune system to said antigen (see page 2, line 15-22 in particular). WO'470 teaches the suppressor cells are obtained from the donor or from the recipient and co-cultured with MSC ex vivo to actually became suppressive. (see page 12 in particular). WO'470 teaches that a transplant is skin, or solid organ (claim 4 and 14,15 in particular) . WO'470 teaches that MSC are human MSC (see page 11 in particular). WO'470 teaches that suppressor cells are administered intravenously, prior to/concurrently with and subsequently with transplantation (see page 10, line 10-25 in particular).

WO'470 does not teach a method for treating a transplant recipient to reducing an immune response of the effector cells against xenoantigen to the effector cells, comprising administering mesenchymal stem cells.

WO'058 teaches a method for enhancing bone marrow engraftment in the individual in need thereof comprising administering to said individual a mesenchymal stem cells (see entire document, Abstract and Claims 1-8 in particular). WO'058 teaches that MSC are administered intravenously, prior to/concurrently with and subsequently with transplantation (see page 2 and 3 in particular). WO'058 teaches that administration of MSC is useful to enhance the effectiveness of transplantation (see page 3 in particular)

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of WO'058 to those of WO'470 to obtain a claimed method for treating a transplant recipient to reducing an immune response of the effector cells against xenoantigen to the effector cells, comprising administering mesenchymal stem cells.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because administration of MSC is useful to enhance the effectiveness of transplantation as taught by WO'058 and can be used in method taught by WO'470 to substitute ex-vivo step of co-culturing T cells with MSC cells by direct in vivo administering of MSC into a transplant recipient. It is also noted that alloantigen taught by WO'470 and xenoantigen of the present application are similar in that both antigens can induce an immune response in the transplant recipient and both differ from antigens expressed by the recipient . It is obvious that WO'470 and present application administer the same treatment to achieve the same results. Therefore it would be obvious to one of ordinary skill in the art at the time the invention was made to substitute one type of an antigen i.e. an alloantigen, to the other type of antigen, i.e. xenoantigen in a process for treating a transplant recipient taught by WO'470. When the prior art method is the same as a method described in the specification, it can be assumed the method will obviously perform the claimed process absent a showing of unobvious property. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Semaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. No claim is allowed.

12. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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